REMARKS

Claims 41, 42 and 55 have been cancelled without prejudice to Applicants' right to prosecute the claimed subject matter in the present application and in related applications. Claims 43, 45, 46, 48, 50, 51 and 54 have been amended. New claims 63-71 have been added. Upon entry of this paper, claims 43, 45-48, 50-54, and 63-71 will be pending and under consideration in this application.

Interview

At the outset, Applicant's representative, Duncan Greenhalgh, wishes to thank Examiners Harris and Eyler for the courtesy extended and for the Examiners' insightful comments during the in-person interview with Duncan Greenhalgh at the Office on December 7, 2004. The substance of the interview is discussed in the Interview Summary provided by the Office on December 7, 2004. In addition, the substance of the interview is incorporated in this paper. As indicated in the Interview Summary, Applicants requested rejoinder of proteins identified by SEQ ID NOs: 1-5, because SEQ ID NO:5 reflects the sequence of the protein U2 snRNP B" and SEQ ID NOs: 1-4 are fragments of U2 snRNP B". The Office agreed that SEQ ID NOs: 1-5 would be searched and examined.

Claim amendments

Applicants have amended claim 43 to remove unnecessary wording and to recite a method wherein the presence of a protein is indicative of the presence of breast cancer in a mammal and wherein the absence of the protein is indicative of the absence of breast cancer in the mammal. Applicants have amended claim 48 to remove unnecessary wording and to recite a method wherein the presence of a complex is indicative of the presence of breast cancer in a mammal and wherein the absence of the complex is indicative of the absence of breast cancer in the mammal. Support for the amendments to claims 43 and 48 is found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; in the first paragraph on page 14; in the last paragraph on page 36; and in original claim 54.

Applicants have amended claims 45, 46, 50 and 51 to alter claim dependency. Applicants have amended claim 54 for consistency with claim 48, from which it depends.

Support for new claims 63 and 67 can be found in the application as originally filed, for example, in original claim 14. Support for new claim 64 can be found in the application as originally filed, for example, in original claim 11. Support for new claim 65 can be found in the application as originally filed, for example, in original claim 12. Support for new claim 66 can be found in the application as originally filed, for example, in original claim 13. Support for new claims 68 and 69 can be found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; in the paragraph bridging pages 11 and 12; in the first paragraph on page 14; in the last paragraph on page 36; and in original claim 54. Support for new claim 70 can be found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; and in original claims 43, 44, 54 and 55. Support for new claim 71 can be found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; and in original claims 48, 49, 54, and 55.

Applicants submit that the amendments introduce no new matter.

The following comments address in order the remaining issues raised in the Office action.

Information Disclosure Statement

During the in-person interview on December 7, 2004, Applicant's representative was informed that the Office had received the Information Disclosure Statements resubmitted to the Office on April 6, 2004. Applicants request that the Office consider the art identified in the PTO-1449 forms and confirm this by initialing each entry on the PTO-1449 forms. Applicants request that the Office then provide a copy of each of the initialed PTO-1449 form for completion of Applicants' files.

Claim Rejections Under 35 U.S.C. § 102(e)

According to section 9 of the outstanding Office Action, claims 41-43, 45-48 and 50-55 presently stand rejected under 35 U.S.C. § 102(e), as allegedly anticipated by U.S. Patent Application Publication number 2002/0081659 ("Rosen"), noting that sequence 687 of Rosen comprises SEQ ID NO: 1 of the present application and that the five hundred forty-fifth paragraph of Rosen mentions breast cancer. Claims 41, 42 and 55 have been cancelled thereby obviating this rejection with respect to these claims. Applicants respectfully traverse this rejection to the extent that it is maintained over claims 43, 45-48 and 50-54, as amended, for the following reasons.

Applicants submit that it is well settled that, for a reference to anticipate a claim under 35 U.S.C. 102(e), the "reference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining...." In re Arkley, 455 F.2d 586, 587 (CCPA 1972) (emphasis in original). A § 102 rejection is "proper only when the claimed subject matter *is* identically disclosed or described in 'the prior art.'" Id. at 587 (emphasis in original). Furthermore, Applicants submit that it is well settled law that a "claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." Amgen v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1354 (Fed. Cir. 2003). See also In re Donohue, 766 F.2d 531 (Fed. Cir. 1985) (holding that a non-enabled disclosure does not constitute prior art under 35 U.S.C. § 102).

Applicants respectfully submit that Rosen does not describe that the protein identified by sequence number 687 is a marker for breast cancer because it fails to point to this particular combination without random "picking, choosing, and combining" from a group appearing to contain four hundred fifty-nine sequences, several hundred possible indications, and four possible uses. Furthermore, because Rosen fails to enable one skilled in the art to make or use a protein identified by sequence number 687 as a marker for breast cancer, it cannot anticipate the present application under 35 U.S.C. § 102(e). Each of these issues is addressed in more detail below.

I. Rosen does not describe that sequence number 687 can be used a marker for breast cancer without random "picking, choosing, and combining."

The Arkley court held that a rejection under 35 U.S.C. § 102 is only proper when "the claimed subject matter *is* identically disclosed or described in 'the prior art.'" Id. at 587 (emphasis in original). The Arkley court further held that for a "rejection under 35 U.S.C. § 102(e) to have been proper, the . . . reference must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." Id (emphasis in original). In reversing a claim rejection under 35 U.S.C. § 102(e), the Arkley court referred to In re Ruschig, 379 F.2d 990 (CCPA 1967), which analogized an invention to a particular tree in a forest and held an application did not describe a particular invention where the application lacked "blaze marks which single out particular trees." Ruschig at 995. In Ruschig, the applicants claimed N-(p-chlorobenzenesulfonyl)-N-propylurea, yet they only disclosed a general class of benzenesulfonylureas with two substituents, one of which can be placed in each of the three positions on the benzene ring. Id. at 991, 994. The Examiner calculated that at least 1,010 compounds were disclosed by this description. Id. at 994. The Ruschig court held, therefore, that "while [...] naming is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required." Id. The appellants argued that "guides" to N-(p-chlorobenzenesulfonyl)-N-propylurea were provided in the specification, for example, by listing one particular substituent together with 18 others. Id. at 995. The Ruschig court found this argument unpersuasive because it did not lead one to conclude that one substituent was preferred to the other 18. Id. at 995. The Ruschig court held, therefore, that N-(p-chlorobenzenesulfonyl)-N-propylurea was not adequately described in the specification and affirmed the rejection of the claimed subject matter. Id. at 995, 996.

Similarly, Rosen does not "clearly and unequivocally" describe that the protein identified by sequence number six hundred eighty-seven is a marker for breast cancer, nor does it guide one skilled in the art to it. To illustrate the analogy with Ruschig, it may be helpful to consider the Rosen reference as describing a method with three independent substituents: a sequence, an

indication, and a possible use. The "substituent" space in Rosen includes four hundred fifty-nine polypeptide sequences, an estimated several hundred indications (listed in paragraphs 425-548), and up to four possible uses for each indication: diagnosis, prognosis, prevention, and treatment. Similar to Ruschig, nowhere in Rosen is sequence number 687 pointed out as associated with breast cancer and nowhere is it indicated that this sequence can be used for the diagnosis (as opposed to prognosis, prevention, or treatment) of breast cancer. "Breast cancer," for example, is listed in paragraph 545 of Rosen which also appears to contain 70 other indications. This particular paragraph alone appears to provide no fewer than 130,356 possibilities (459 sequences x 71 indications x 4 uses). Applicants estimate the total number of possible indications listed between paragraphs 425-548 of Rosen application to be several hundred. Conservatively, Rosen appears to teach at least several hundred thousand different possibilities.

Applicants submit that Rosen does not reasonably lead a person skilled in the art to any particular sequence associated with either diagnosis, prognosis, prevention, or treatment of any particular indication without random "picking, choosing, and combining." In fact, Rosen fails to provide guidance to a single combination of the elements discussed above. Applicants fail to see any "blaze marks" provided in the Rosen application that would lead anyone to reasonably believe that sequence number 687 was "preferred" as a tool for detection of breast cancer. In contrast to Rosen, the present application "clearly and unequivocally" identifies the use of protein of SEQ ID NO: 5 and fragments thereof (namely the proteins of SEQ ID NO: 1-4) as markers for breast cancer.

Because the Rosen application does not "clearly and equivocally" describe diagnosing breast cancer in a mammal using a protein comprising any of SEQ ID NOS: 1-5 as a marker, Applicants submit that the Rosen application cannot anticipate the claimed invention.

II. Rosen does not enable the use of any of Applicants' SEQ ID NOs:1-5 as a marker for breast cancer.

For a reference to be enabling, it is well settled that a person skilled in the art should be able to practice the invention without "undue experimentation." MPEP 2164.01. See also In re Wands, 858 F.2d 731 (Fed. Cir. 1988). The factors courts consider when determining whether experimentation is "undue" include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. MPEP 2164.01(a).

When this test is applied to Rosen, Applicants submit that Rosen clearly does not enable one skilled in the art to practice using an amino acid sequence comprising any of Applicants' SEQ ID NOs: 1-5 as a marker for breast cancer without "undue experimentation." Addressing factors (A) and (B), Applicants submit that in order for Rosen to anticipate the claimed invention, Applicants submit that Rosen needs to identify the use of a protein comprising any of Applicants' SEQ ID NOs: 1-5 as a marker for breast cancer. As discussed in section I, Applicants submit that Rosen fails to do this. Addressing factor (F), Rosen provides no direction concerning the use of sequence number 687, Rosen's amino acid sequence apparently comprising Applicants' SEQ ID NO:1, or any other sequence comprising any of SEQ ID NOS: 1-5 as a marker for breast cancer. As discussed above, there are at least hundreds of thousands of possible combinations of sequences, possible indications, and possible uses based on the teachings of Rosen, and that there is no teaching whatsoever leading the skilled artisan to combine the protein of sequence number 687 and breast cancer diagnosis. Addressing factor (G), there are no working examples of the use of a protein comprising any of Applicants' SEQ ID NOs:1-5 as a breast cancer marker. There is not even a prophetic example that the protein of sequence 687 can be used as a breast cancer marker. Addressing factor (H), in view of the absence of specific guidance in Rosen pointing specifically to the use of a protein comprising any of Applicants' SEQ ID NOs:1-5 as a breast cancer marker, Applicants submit that the quantity of

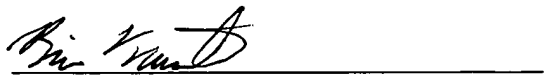
experimentation needed to practice the present invention based on the content of the Rosen disclosure is very large, as one of skill in the art would need to test each sequence disclosed in Rosen for each recited possible indication and for each recited possible use before learning which combinations were of any use. Addressing factors (C)-(E), Applicants submit that based on the level of ordinary skill in the art, the state and unpredictability of the art, and the lack of direction provided by Rosen, the usefulness of a protein comprising any of Applicants' SEQ ID NOs:1-5 as a breast cancer marker was not predictable absent the specific teachings of the present application. Applicants submit, therefore, that Rosen does not enable one skilled in the art to use a protein comprising any of Applicants' SEQ ID NOs:1-5 as a marker for breast cancer as required by Amgen and, therefore, does not qualify as prior art under 35 U.S.C. § 102(e).

In summary, Applicants respectfully submit that Rosen does not qualify as an anticipatory reference under 35 U.S.C. § 102(e) because it does not describe the invention as required by Arkley, and because it does not enable the invention as required by Amgen. Accordingly, Applicants respectfully request that the rejection of pending claims 43, 45-48, and 50-54 be reconsidered and withdrawn.

CONCLUSION

Applicants believe that the claims are in condition for immediate allowance. The Examiner is invited to telephone the undersigned attorney to discuss any remaining issues.

Respectfully submitted,



Date: December 14, 2004
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